



Attorney Docket No. 24871

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Shulov AHARON and Naftali PRIMOR

Serial No.: 10/030380

Art Unit: 1654

Filed: July 25, 2002

Examiner: Randall WINSTON

For: **ANALGESIC FROM SNAKE VENOM**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Declaration under 37 CFR 1.132

1. I, Naftali Primor, declare and say:

1.1. That I am a citizen of Israel, residing at Gelber 16 St. Apt. 21 Jerusalem,

1.2. That I am an inventor of the captioned application for U.S. Letters Patent.

1.3. That, I have studied :

Hebrew University of Jerusalem – BSc. 1968 – 1971 Zoology and Physiology.

Hebrew University of Jerusalem – MSc 1971 – 1973 Life Sciences.

Hebrew University of Jerusalem – PhD 1978 Life Sciences.

1.4. Professional background :

2000 – Present : Director of Research and Development at Shulov Institute For Sciences (SIS).

1984 – 2000 : Scientist in company specializing in the development of natural occurring substances. (SIS)

1984 – 1986 : Scientist – International Genetic Science Partnership, Jerusalem Israel.

1982 -1986 : Toxicologist. Principal Investigator on Office of Naval Research (ONR), USA. The Grant was carry out at The New York Aquarium and Osborn Laboratories of Marine Sciences, Coney Island, Brooklyn, N.Y, 11224.

1979 -1982 : Associated Research Scientist. Principal Investigator on ONR Grant. New York University Medical Center, NY, USA.

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1978 : PhD Thesis awarded with distinction. Thesis on snake venom fractions effective on insects.

1973 : Pre-Doctoral Trainee, Facultat De Medicina, Biochemic, Marseille, France.

1.5. I am currently involved in several projects involving snake venom, analgesics, pharmaceuticals, and biotechnology, all of which are at various stages of development. I have been investigating snake venom, its components, and physiological response for many years and I am well cognizant of both the research and the clinical practice on the subject.

1.6. I am fully conversant with inhibitor compounds that inhibit zinc-dependent metalloproteinases associated with pathological conditions including the subject matter of United States Patent No: 6,057,297 issued on May 2, 2000 to Politi et al. (hereinafter "Politi et al.") which describes synthetic inhibitor compounds of zinc-dependent metalloproteinases.

2. Regarding Politi et al. US Patent No: 6,057,297, I have the following remarks:

2.1 I have intensively studied the Official Action dated November 15, 2005 as well as Politi et al. I am aware that the examiner has rejected claims 1-3, 5, and 8-18 under 35 U.S.C. 103(a) as being unpatentable over Politi et al.

2.2 The Politi et al. patent describes synthetic peptidomimetic compounds that inhibit zinc-dependent metalloproteinases associated with pathological conditions. In my expert opinion, Politi et al. fails to describe a component isolated from snake venom that is non-toxic and has an analgesic effect after a lag period. Further, in my expert opinion Politi et al. not only fails to contain any description or suggestion that would lead an artisan to the presently claimed product and method of use, but in fact, contains a description that would lead the artisan away from the presently claimed product and method of use.

In the November 15, 2005 Official Action, Examiner Winston asserts that the Politi et al. product appears to be the same as the presently claimed product because the Politi et al. product is a non-toxic venom product that has pharmaceutical activity that relates to pain relief. The Examiner points to col. 4, lines 14-18; col. 3, lines 52-55; and Example 8; of the Politi et al. reference in support of his position.

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Politi et al., at col. 4, lines 14-18, describes that small peptides isolated from snake venom may have the job of inhibiting metalloproteinases, but that such components have extremely specialized activity unlike the Politi et al. synthetic compounds which exhibit "much higher inhibiting activity" (approximately 1000 times). This passage clearly states that the synthetic inhibitors of Politi et al. are *significantly* different from small peptides isolated from snake venom. Further, nowhere does this passage suggest that such snake venom isolates exhibit analgesic activity. In addition, it is my opinion that an investigator reading this passage would have no motivation to explore such small peptides isolated from snake venom for non-toxic analgesic activity.

In complete contrast to the Examiner's cited position regarding Politi et al., Politi et al. in fact describes in Example 8, that a number of *toxic hemorrhagins*, i.e., zinc-dependent metalloproteinases, were extracted from snake venom. See Example 8 at col. 16, lines 46-48. Thereafter the synthetic inhibitors were added to the isolated hemorrhagins and inhibitory activity was determined. See col. 17. Nowhere is it suggested or described in Example 8 that the isolated hemorrhagins are non-toxic, let alone have an analgesic effect.

Furthermore, at Col. 3, lines 52-60, Politi et al. describe that zinc-dependent metalloproteinases are pathological agents. Politi et al. does not describe that zinc-dependent metalloproteinases are non-toxic and exhibit an analgesic effect. In contrast, we claim a non-toxic fraction isolated from snake venom that has an analgesic effect. The zinc-dependent metalloproteinase pathological agent described in Politi et al. cannot be a non-toxic fraction that has an analgesic effect.

- 2.3 In conclusion, in my expert opinion, the Politi et al. reference relates to synthetic inhibitors of zinc-dependent metalloproteinase pathological agents and not to non-toxic fraction isolated from snake venom that has an analgesic effect as set forth in my application.
3. The undersigned Declarant declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; further that these statements were made with the knowledge that willful false

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statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the application or any patent issuing thereon.

Signed at
Israel,

January 31, 2006

Naftali Primor

Naftali PRIMOR

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